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# Emotional and Clinical Challenges of Delayed HIV Seroconversion

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Abstract

**Aims:** to examine the emotional and clinical impact of delayed HIV seroconversion in a 36-year-old male healthcare professional in Ecuador.

**Methodology:** a case report analysis that included patient history, clinical presentation, and treatment outcomes.

**Results:** severe anxiety, depression, and perceived risk of death due to delayed ART initiation. Symptoms of weight loss and profuse sweating resolved after ART and psychiatric treatment.

**Scientific Novelty:** the paper highlights the complexities of delayed HIV diagnosis and its profound emotional impact, emphasising the need for regular testing and comprehensive mental health support.

**Conclusion:** timely HIV testing and integrated medical and emotional care are critical for managing delayed seroconversion.

Keywords: HIV; HIV-1; HIV infection; HIV testing; seroconversion; HIV seropositivity; AIDS serodiagnosis.

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## Introduction

HIV infection progresses through multiple stages and eventually compromises the immune system. Antiretroviral therapy (ART) is typically recommended for AIDS diagnosis or when CD4 counts drop, according to previous studies [1–4]. Early initiation of ART is crucial and often accompanied by psychological challenges [5, 6]. A 36-year-old healthcare professional in Ecuador experienced gastrointestinal issues, HIV diagnosis, and emotional distress. Unresolved grief from family loss and revealing his bisexuality after seroconversion added complexity. Despite advancements in understanding and acceptance of sexual orientation in society, studies have shown that individuals in Ecuador still face challenges in accepting their sexual orientation, leading to increased emotional stress. Effective evaluation, continuous testing, and mental health assistance are crucial for individuals diagnosed with HIV.

Murphy et al. (2023) stressed the importance of holistic HIV management approaches, emphasising the impact of emotional support and timely ART initiation on well-being [7]. This case integrated literature on delayed

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seroconversion and HIV's emotional impact, contributing to a broader understanding of effective HIV management, enhancing clinical practice, and offering insights for future diagnoses among at-risk populations.

## Case Presentation

### *Background*

The case of a 36-year-old male healthcare professional in Ecuador is significant due to the intricate relationship between delayed seroconversion, severe emotional distress, and physical symptoms he experienced. The patient, who recently accepted his bisexuality, experienced an acute diarrheal episode in September 2022, leading to an indeterminate HIV test result, which became reactive three weeks later. During this period, he faced substantial anxiety and an elevated perceived risk of mortality due to the delayed initiation of antiretroviral therapy (ART), compounded by financial constraints and ineligibility for pre-exposure prophylaxis (PrEP) as per the Ecuadorian Social Security and Ministry of Public Health regulations.

Despite testing negative for opportunistic infections, the patient experienced severe physical symptoms, including a 2 kg weight loss during the diarrheal episode and an additional 10 kg weight loss following the indeterminate HIV test result (Table 1). These symptoms were accompanied by generalised anxiety and a profound sense of impending doom. Initial laboratory findings during the diarrheal episode revealed leukocytosis and lymphopenia, with a stool culture that did not isolate any pathogens. Treatment with intravenous ceftriaxone for three days and oral ciprofloxacin for five days improved the diarrhoea symptoms.

The patient's emotional state was significantly affected during the period of seroconversion and before ART initiation. He has been undergoing treatment for post-grief depression since 2020, following the deaths of his maternal grandmother in 2018 and his father in 2020 due to COVID-19. This unresolved grief compounded his anxiety during the HIV diagnosis. The delay in receiving CD4 and viral load results, which postponed the start of ART, was a major contributor to his anxiety. Additionally, the indeterminate HIV test result in October followed by a reactive result in November caused further emotional turmoil. The fourth-generation test results, which were only slightly reactive, were added to the uncertainty and distress. The individual also struggled with the task of disclosing their sexual orientation to co-workers and worrying about being judged for not taking precautions during their exploration of their sexuality. This fear was compounded by the fact that he had engaged in unprotected sex, leading to feelings of guilt and self-disappointment, particularly as an HIV specialist. His family supported his healthcare but not his sexual orientation, adding another layer of emotional strain.

Despite these challenges, the patient received crucial emotional and psychological support from friends, family members, and colleagues. This support helped mitigate his post-grief depression and fostered the self-care. His colleagues also pressured him to expedite his test results so that he could receive appropriate HIV and psychiatric treatments. Additionally, psychological and spiritual counselling provided significant relief, helping him to manage his anxiety and depression. The patient adhered to cognitive-behavioural therapy (CBT) to address severe insomnia, which worsened the following diagnosis. His psychiatric treatment involved quetiapine and fluoxetine, which later transitioned to sertraline and clonazepam owing to the unavailability of fluoxetine and limited improvement in his moderate depression. Over six months, his emotional state significantly improved. The support from his mother, whom he supported financially, played a crucial role in his recovery.

Currently, the patient adheres to his ART regimen, maintaining an undetectable viral load and CD4 count of 717 cells/mm³. He remains under regular psychological and psychiatric follow-up. Although he gained weight due to discontinuing gym activities, he expressed a desire to resume physical exercise, but struggled with motivation. He wishes to discontinue psychiatric medication, but remains adherent until his psychiatrist advises cessation. The patient continues to find it challenging to openly maintain relationships due to societal norms in traditional Ecuador, and he has not received PrEP because it is only available for serodiscordant couples according to Ecuador's Ministry of Public Health guidelines.

### *Research Problem*

The results of this case highlighted the critical necessity of continuous HIV testing and extensive evaluation, even when the initial outcomes are negative or uncertain. Addressing mental health concerns of individuals with HIV is a vital component is an essential element of holistic care. The patient's narrative emphasises the need for a healthcare strategy that addresses both the medical and emotional aspects to promote overall well-being.

### *Objectives*

- This emphasises the necessity of consistent HIV testing for individuals with inconclusive or negative initial findings.
- Advocating for mental well-being is a crucial aspect of HIV-positive patient care.
- Promoting a holistic healthcare approach encompassing medical and emotional components.

## Methodology

### *General Background*

The objective of this case report was to investigate the challenges in diagnosing patients with HIV and their emotional consequences. This case aimed to provide insight into the emotional and psychological reactions of patients upon receiving their diagnosis and commencing antiretroviral therapy (ART) within Ecuador's healthcare system.

### *Study Design*

o This observational, retrospective, analytical, and qualitative case report focused on the journey of a single patient from diagnosis to treatment. It examined the emotional and psychological responses that result from delays in ART initiation. This approach enabled the case to address the specific challenges faced by patients and emphasised the broader implications for HIV care, particularly in resource-limited settings, such as Ecuador.

### *Participants*

o The case report involved a 36-year-old male healthcare professional who was HIV-positive. As this was a case report, no inclusion or exclusion criteria were applied. The patient provided a comprehensive overview of his demographic and clinical features, including the severe anxiety and weight loss associated with his condition.

### *Interventions/Variables*

The primary intervention in this report was the initiation of antiretroviral therapy (ART) for an HIV-positive patient following the confirmation of his status. During the first semester of follow-up, prophylaxis for *Pneumocystis jirovecii* pneumonia (PCP) and Candida was initiated because of a CD4 count of 150 cells/μL. The patient received continuous psychological support, nutritional counselling, and pharmaceutical guidance to ensure adherence to the treatment regimen.

### *Data Collection*

Data were collected through a review of patients' medical records, including HIV testing results, viral load measurements, CD4 counts, and screening for opportunistic infections. Detailed interviews were conducted in order to evaluate patients' emotional and psychological states. These interviews, which were conducted retrospectively, captured the patients' experiences during and after seroconversion. Regular medical evaluations and psychological assessments are integral to understanding a patient's overall well-being.

### *Data Analysis*

Descriptive statistics were used to analyse the clinical data, providing a detailed overview of the patient's health status and progression of his condition over time. A systematic evaluation of laboratory results was conducted using standard medical software to ensure precise data analysis. Qualitative data from psychological assessments were thoroughly examined using thematic analysis in order to identify patterns in the patients' emotional and psychological responses. Software tools, such as SPSS for quantitative data and NVivo for qualitative data, were used to facilitate this analysis.

### *Ethical Considerations*

Ethical considerations involved securing informed consent from the patients and following rigorous confidentiality measures. The study was approved by the hospital's ethics committee where the research was conducted.

### *Limitations*

The main limitations of this report included its focus on a single case, which limited the generalizability of the findings. Additionally, the limited availability of reagents and medications in the reporting setting might have influenced the results. Nonetheless, this report provided valuable qualitative insights into the emotional experiences of HIV patients in resource-limited environments.

## Results

This case report provides a comprehensive overview of HIV diagnosis and management, highlighting the intricate processes involved. As shown in Table 1, the patient's HIV infection progressed from indeterminate and reactive results initially to effective viral suppression and substantial enhancement of CD4 counts following the commencement of antiretroviral therapy (ART).

Table 1. Serological, Confirmatory, and Control Test Results

| Date | HIV Test | Viral Load (copies/mL) | CD4 Count (cells/mm³) | Tuberculosis Sputum Smear | Histoplasma Culture | *P. jirovecii* Culture |
|---|---|---|---|---|---|---|
| July 2022 | Non-reactive | - | - | - | - | - |
| August 2022 | Non-reactive | - | - | - | - | - |
| November 16, 2022 | Indeterminate | - | - | - | - | - |
| November 20, 2022 | Reactive | - | - | - | - | - |
| November 25, 2022 | - | 105,156 | 167 | Negative | Negative | Negative |
| March 2023 | - | <40 | 426 | - | - | - |
| June 2023 | - | Not Detectable | 469 | - | - | - |
| Feb 2024 | - | Not Detectable | 717 | - | - | - |

The initial indeterminate HIV test result in November 2022 was followed by a reactive result a few days later, illustrating delayed seroconversion. Subsequent ART initiation led to undetectable viral load levels and significant improvement in CD4 counts over the following months.

## Discussion

The emotional experience of the patient during his transition from HIV-negative to HIV-positive underscored the importance of addressing both the medical and psychological aspects of HIV management. This case illustrated the intricacies involved in diagnosing and managing HIV infection, particularly in cases where seroconversion occurs at a later stage.

The onset of primary HIV infection can be divided into two phases: acute infection within the first 30 days and recent infection within 180 days (6-12 weeks). During this period, individuals may be asymptomatic or experience non-specific symptoms, such as fever, headache, and malaise, which could be mistaken for other illnesses [1–4, 8]. Serological tests that detect both HIV-1 antibodies and the p24 antigen generally become positive 2–3 weeks after infection [3, 4]. In cases where HIV-1 RNA detection is available, positive results can be obtained within 7 to 10 days [2–4, 9, 10]. Additionally, early initiation of ART can also improve long-term outcomes by reducing the likelihood of developing drug resistance and delaying disease progression. Discontinuing ART during this phase is not typically recommended because there are no proven methods to avert viral rebound in most patients [1, 3, 4].

The delayed seroconversion observed in this clinical case raises concerns regarding the dynamics of HIV infection and diagnosis. Unlike most cases of PHI, where seroconversion typically occurs within a few weeks of viral exposure, seroconversion in this patient occurred later, after a severe diarrheal episode in September 2022 [9–12]. The unusual delay in seroconversion suggests that the HIV infection in this patient may have been atypical in terms of viral replication and immune response [1, 3, 4]. The precise reasons for the delay in seroconversion remain uncertain, although it may be linked to the unique interplay between the virus and the individual's immune response. In rare cases, HIV may exhibit slower and less aggressive viral replication, which could delay the detection of specific antibodies in conventional diagnostic tests [9–12].

This delay in seroconversion emphasises the importance of continuous surveillance and regular HIV testing, especially in individuals with a potential risk of exposure [1, 3, 4]. This case underscored the potential danger of HIV seroconversion going unnoticed because of the scarcity of available diagnostic reagents and financial limitations at the time. It also raises interesting questions regarding the possible link between severe gastrointestinal symptoms and HIV infection. Although a definitive causal relationship cannot be established, it emphasises the need for healthcare professionals to consider the possibility of HIV infection in patients with compatible symptoms, even if seroconversion does not occur promptly [8,13].

Fourth-generation immunoassays are highly sensitive and specific for identifying established HIV-1 and HIV-2 infections, with a range of 99.7% to 100% [3, 4, 14]. However, they have low efficacy in detecting primary HIV infection, ranging from 54% to 83%, particularly in individuals with acute HIV infection who have negative results for HIV-1 by western blotting, but are reactive to HIV-1 NAT. Research suggests that fourth-generation IAs typically become positive within 5.3-7.4 days of detecting HIV-RNA and approximately 13-23.6 days (median 17.8) post-infection [8]. A simulation model indicated that 99% of HIV-infected individuals will be detectable by fourth-generation IAs within 45 days post-exposure [13].

When choosing the initial ART regimen for adults who have not previously taken ART, it is important to consider factors such as HLA-B*57:01 status, HBsAg status, as well as personalized evaluations of cardiovascular risk and weight, especially if considering DTG. Additionally, alternative regimens such as TDF/XTC + DTG, TAF/FTC, or

TDF/XTC + RAL are based on patient characteristics such as weight gain, prodrug type, and potential renal and bone toxicity [3, 4, 15]. These assessments should be conducted alongside dosing requirements for TAF and RAL to ensure the selection of the most appropriate and effective treatment regimen for each patient's unique needs [3, 4].

Recent research has highlighted the importance of the NLRP3 inflammasome in HIV infection. Different mechanisms, such as ion flow, mitochondrial release of oxidative radicals, and lysosomal damage, are thought to activate this pathway [16]. HIV-1 envelope glycoproteins bind to CD4 and its coreceptors (CXCR4/CCR5), which activate pannexin-1 hemichannels and increase extracellular ATP and potassium efflux through purinergic receptors (P2Y2) [17]. This process is crucial in the early stages of HIV infection, as P2Y2 receptors interact with NLRP3 in the virological synapse between infected and uninfected target cells, facilitating NLRP3 activation, which is vital for regulating viral entry into target cells, and its levels increase rapidly during infection [18]. Chronic HIV infection causes inflammation and tissue damage by activating the NLRP3 inflammasome through Tat and Vpr proteins in lymphocytes, microglial cells, and macrophages [19–21].

The P2Y2 receptor is crucial for HIV-1 entry, as it facilitates plasma membrane depolarisation through PYK2 activation, promoting the early fusion of HIV-1 with target cells. Additionally, NLRP3 inflammasome modulates F-actin polymerization and inhibits cytoskeletal remodelling, which is essential for viral entry. However, HIV-1 has evolved mechanisms to evade NLRP3, including post-transcriptional degradation via ubiquitination [18]. P2X7 receptors in HIV-infected macrophages are noteworthy in the CNS as they facilitate the release of virions from VCCs without causing cell death, making them promising therapeutic targets for accessing HIV reservoirs [17, 22–24]. Genetic variations, such as NLRP3 and IL1B, can offer protection against HIV infection, while variants in the IL18 promoter increase susceptibility to it [25–28]. NLRP3-mediated caspase 1 activation in CD4 T cell pyroptosis depletes CD4 T cells, causing sustained inflammation and contributing to disease progression and complications, including cardiovascular and neurological diseases [26, 29–31].

Dolutegravir, an integrase strand transfer inhibitor, boasts numerous benefits, including its compact size, approval for use in paediatric oral suspensions, a strong genetic resistance barrier, and minimal drug interactions. However, it has certain limitations, including the need for baseline pharmacogenetic testing to assess the risk of abacavir hypersensitivity and a larger pill size. In 2019, the FDA approved DTG/3TC for HIV treatment, eliminating the need for HLA-B5701 testing with its NRTI fixed-dose combination [19, 21, 32–37].

HIV drug resistance monitoring in infants is essential, particularly given the increasing use of DTG-based antiretroviral therapy. A recent case of DTG resistance was reported in a HIV-positive infant born to a mother receiving DTG-based ART in Haiti. To prevent DTG resistance, pretreatment HIVDR surveillance among treatment-naive infants is necessary, and prompt implementation is crucial as the use of DTG-based ART increases. The World Health Organisation (WHO) recommends DTG-based ART as the preferred choice for both first- and second-line treatments, with over 25 million individuals currently benefiting from it. However, the recent data show that HIVDR to DTG is becoming a concern at levels higher than those observed in clinical trials. Studies have reported DTG resistance levels ranging from 3.9% to 8.6%, with levels as high as 19.6% among individuals with high HIV viral loads who have had extensive treatment experience and have transitioned to DTG-containing ART [32, 37, 38].

Although cabotegravir has shown great effectiveness in preventing HIV infection through pre-exposure prophylaxis (PrEP), recent cases of resistance to integrase strand transfer inhibitors (INSTIs) have been reported, particularly in individuals who were later diagnosed with HIV after exposure to CAB-LA. This could result in the emergence of drug-resistant mutations associated with INSTIs. However, despite these concerns, the benefits of using CAB-LA for PrEP outweigh its potential risks and it is necessary to continue its implementation. To address the issue of drug resistance, it is crucial to establish standardized surveillance among individuals who test positive for HIV while receiving PrEP [19, 37–41].

The patient experienced significant anxiety, 10 kg weight loss, and a sense of impending doom during the seroconversion period due to the lack of immediate ART. CBT was initiated to provide emotional support and address social prejudices related to patients' sexual orientation. The patient's primary concern was the potential impact of delayed treatment on his viral load and CD4 count given his professional expertise in HIV. This highlights the importance of timely ART initiation to alleviate anxiety among healthcare professionals diagnosed with HIV. Delays in accessing ART can significantly impact both individual and public health outcomes, emphasising the need for early intervention and continuous monitoring [42].

The patient's psychiatric treatment regimen involved fluoxetine, quetiapine, and clonazepam, with sertraline substituted due to the unavailability of fluoxetine. Emotional support from his family and colleagues significantly contributed to his emotional recovery, emphasising the importance of a supportive social network and professional environment in managing the psychological aspects of living with an HIV infection. Late presenters can achieve viral suppression but often face challenges with immunological recovery, highlighting the need for accessible and comprehensive care to address both medical and psychological needs [43].

## Conclusions and Implications

This case highlighted the intricate nature of diagnosing and managing Primary HIV Infection (PHI), especially when seroconversion is time-consuming. The patient's severe diarrhoea and fever, followed by an indeterminate HIV test result and eventual diagnosis, emphasised the need for continued surveillance and periodic testing in individuals who may have been exposed to HIV. A comprehensive healthcare strategy that included both the medical and emotional aspects of care was necessary to provide holistic support to the patient.

### *Impact*

Additional research is required to better understand the phenomenon of delayed seroconversion in HIV infection and its relationship with severe gastrointestinal symptoms.

In order to improve the diagnostic accuracy, new diagnostic tests are needed during the acute phase of HIV infection. Healthcare providers should exercise caution when screening for individuals with a history of high-risk exposure or symptoms indicative of HIV infection.

Providing psychological support is crucial in care plans for patients who test positive for HIV.

This case highlighted the importance of adopting a holistic approach to HIV management that encompasses both medical interventions and emotional support. These findings emphasize the importance of ongoing monitoring and regular HIV testing to ensure timely diagnosis and treatment, ultimately leading to improved health outcomes for patients.

## Declarations

### *Author Contributions*

Conceptualization, FCGG; methodology, FCGG; investigation, FCGG, FCS, FCHR; resources, FCGG; data curation, FCHR.; writing—original draft preparation, FCGG. And FCS; writing—review and editing, FCGG, FCHR; visualization, FCS; supervision, FCGG; project administration, FCGG; All authors have read and agreed to the published version of the manuscript.

### *Data Availability Statement*

Data sharing was not applicable, and no new data were created or analysed in this case report.

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### Institutional Review Board Statement

Ethical review and approval were waived because of the observational nature of the case, which involved no additional risks or experimental interventions. This case report focuses on the analysis of clinical data from a standard treatment. Confidentiality was ensured by anonymizing patient data, and the research adhered to privacy regulations. The findings aim to enhance the understanding of atypical HIV presentations and improve clinical practice.

### Informed Consent Statement

Informed consent was obtained from the patient for inclusion of medical and clinical information in this case report.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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